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Combined proton-photon treatments: How can limited proton slots be optimally distributed over a patient cohort?

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Introduction: Although rapidly growing, proton therapy is a limited resource, which is not available to all the patients who may benefit from it. In this study, we investigate if combined proton-photon treatments, in which some fractions are delivered with protons and the rest with photons, improve on single-modality treatments. Combined treatment can be motivated by the consideration that, on the convex part of the NTCP curve, the first proton fractions are the most beneficial. We assume a situation of limited proton slot availability and develop methods to distribute those limited slots over a patient cohort optimally in order to optimize the benefit of proton therapy at a population level.

Material and Methods: We consider a cohort of 45 head and neck cancer patients for which IMRT and IMPT plans were previously created [1]. NTCP models for relevant side effects (e.g. xerostomia) were used to calculate the NTCP values for all the plans. We investigate a 30 fraction simultaneous integrated boost (SIB) scheme (1.8 Gy to the PTV, 2.3 Gy to the GTV) and a sequential boost (SEQ) scheme with a 25 fraction base plan (2 Gy to the PTV) and a 10 fraction boost plan (2 Gy to the GTV). Under the assumption that, due to limited resources, only a small percentage of the total number of fractions can be delivered with protons, an integer programming algorithm was applied to determine the optimal number of proton fractions per patient that minimizes the total number of expected complications over the patient cohort.

Results: Figure 1a shows the NTCP values for xerostomia in the IMRT and IMPT plans for the SIB scheme for all patients. Figures 1b shows the optimal allocation of proton slots for the situation where 20% of all fractions are delivered with protons. The patients with the highest ΔNTCP value (IMRT-IMPT) receive the largest number of proton fractions. The average xerostomia NTCP value from all 45 patients for the SIB scheme for combined treatment equals 13.0%. For the single-modality treatment, where the 20% of patients with the highest ΔNTCP are selected for proton therapy, the average NTCP equals 13.2%. For the SEQ scheme, the average NTCP values for xerostomia equal 13.6% and 14.2% for the combined and the single-modality treatment, respectively. Figure 1c shows the corresponding proton slot allocation for the SEQ scheme, indicating that only 3 patients receive proton slots for the boost plan whereas most proton slots are used for base plans. To achieve an average NTCP of 14.2%, combined treatment would require only 265 (16.8%) proton fractions instead of 315 (20%). Similar results were obtained for NTCP models for dysphagia and aspiration.

Conclusion: Combined proton-photon treatments with optimized allocation of proton slots increase the benefit of proton therapy on the population level compared to single-modality treatments with optimal proton patient selection. However, the benefit is small for the SIB scheme. A larger benefit is observed for the sequential boost scheme, where combined treatments can exploit that some patients benefit from proton boost plans and others from proton base plans.

[1] A. Jakobi et al., Identification of Patient Benefit From Proton Therapy for Advanced Head and Neck Cancer Patients Based on Individual and Subgroup Normal Tissue Complication Probability Analysis, IJROBP, V. 92(5), pp.1165-74, 2015

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